REMARKS

Claims 14 and 20 are pending. Claims 15 and 31 have been canceled without prejudice or disclaimer and solely for the purpose of expediting prosecution. Claims 3-6, 8-9, 12-13, 16-19, 21-22, 24-25, and 27-28 were previously canceled. Claims 1-2, 7, 10-11, 23, 26, and 29-30 are withdrawn. Claims 14 and 20 have been amended to recite that the isolated recombinant megakaryocyte tyrosine kinase 1, or fusion protein thereof, has the amino acid sequence of SEQ ID NO. 2. Support for this amendment is found throughout the specification; see, for instance, the legend for Figure 9 at page 9 of the specification and the third and fourth paragraphs of page 13.

II. Applicants overcome the Examiner's rejections

1. The Examiner states that "[T]he title of the invention is not descriptive." Office Action at page 2. Applicants have amended the title to reflect that the claimed invention is directed to a "Novel Megakaryocytic Protein Tyrosine ~~Kinases~~ Kinase 1."

2. The Examiner states that "[T]he abstract of the disclosure is objected to because the abstract is in two paragraphs." Office Action at page 2. Accordingly, Applicants have combined the two paragraphs into one and have appended a clean copy of the abstract, on a separate sheet, to this paper.

3. Applicants have amended page 1 of the specification to relate the lineage of the present application, *i.e.*, that it is a divisional application of U.S. application serial no. 08/232,545, filed on April 22, 1994, now U.S. patent No. 6,506,578. Applicants also have submitted an Application Data Sheet conveying this lineage.

4. The Examiner rejected claims 14, 15, 20, and 31 under 35 U.S.C. § 112, second paragraph for (a) reciting "an isolated recombinant MKK1" in claim 14; (b) reciting Figures 1A, 1B, and 1C for the sequence of MKK1 in claim 15; and (c) for reciting "MKK1 protein." Office Action at page 3.

Applicants have amended the claims to recite a "megakaryocyte tyrosine kinase 1" and to specify that the megakaryocyte tyrosine kinase 1 protein has the amino acid sequence

of SEQ ID NO. 2. For these reasons, Applicants respectfully request that the Examiner withdraw these rejections.

5. The Examiner rejected claims 14 and 20 under 35 U.S.C. § 112, first paragraph as lacking written description, because "the specification does not disclose all the MKK1 polypeptides." Office Action at page 4.

Applicants have amended claims 14 and 20 to recite that a megakaryocyte tyrosine kinase 1 protein has the amino acid sequence of SEQ ID NO. 2, for which there is sufficient written description support. The Examiner acknowledges that "the specification discloses MKK1 polypeptide of SEQ ID NO. 2. This meets the written description and enablement provisions of 35 U.S.C. § 112, first paragraph" (emphasis added; Office Action at page 4). Accordingly, Applicants submit that there is written description for the presently claimed invention and respectfully request that the Examiner withdraw this rejection.

6. The Examiner rejected claims 14 and 20 under 35 U.S.C. § 112, first paragraph as lacking enablement because "the lack of description of the various MKK1 forms in the specification does not enable one of skilled in the art [to] make and/or use the invention." Office Action at page 6.

Applicants' amendment overcomes the rejection for the reasons cited in the previous subsection, which also is in keeping with the Examiner's acknowledgement that an MKK1 of SEQ ID NO. 2 is enabled. See page 7 of the Office Action. Accordingly, Applicants submit that the presently claimed invention is enabled and respectfully requests that the Examiner withdraw this rejection.

7. Claims 14 and 15 are rejected under 35 U.S.C. § 102(a) as being allegedly anticipated by Bennett *et al.*, *J. Biol. Chem.*, 269(2), pp. 1068-74, January 14, 1994, or Sakano *et al.*, *Oncogene*, 9(4), pp. 1155-61, April, 1994. Office Action at pages 8 and 9.

Applicants have filed herewith a declaration executed by Ricardo Martinez, a research scientist who was employed at Sugen, which is a collaborator of the assignee of the present application (Max-Planck). Dr. Martinez attests that he sequenced the claimed megakaryocyte

tyrosine kinase 1 before the publication date of Bennett *et al.* Since the declaration antedates both of the cited references, neither is available as prior art against the present claims. Accordingly, none of the claims are anticipated and, thus, this rejection is moot.

8. Claims 20 and 31 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Bennett *et al.*, *supra*, or Sakano *et al.*, *supra*, in view of Maniatis *et al.*, 1982, pages 422-430. Office Action at page 9.

For the reasons cited in the preceding subsection, Ricardo Martinez's declaration evidences Applicants' isolation and identification of the DNA and amino acid sequences of megakaryocyte tyrosine kinase 1 prior to Bennett *et al.* and Sakano *et al.* Accordingly, neither may be combined with the referenced Maniatis publication. Therefore, none of the claims are rendered obvious and, thus, this rejection is moot.

III. Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date March 2, 2004

By _____

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5475
Facsimile: (202) 672-5399

Beth A. Burrous
Attorney for Applicant
Registration No. 35,087

PROJECT______

Map Draw Analysis of ORF

[redacted]

Page 1

MKK1-3 consensus 4/12 Map (1 > 2053)Site and Sequence
Enzymes : All 335 enzymes (No Filter)
Settings: Linear, Certain Sites Only, Standard Genetic Code

```
GTGCAGCGGGACGCTCGGGTGTGCAGCCGGCTCGCGGAGGCCTCCTGGGGGGGGGSGCSCGGGCGCGGCT 70
CACGTCGCCCTGCGAGCCCACACGTCGGCCGAGCGCCTCCGGAGGACCCCCCCCCSCGSGCCCGCGCCGA

Only_once > Below
SUG#301
< SUG#313

 V  Q  R  D  A  R  V  C  S  R  L  A  E  A  S  W  G  G  ?  ?  G  R  G
  C  S  G  T  L  G  C  A  A  G  S  R  R  P  P  G  G  G  ?  ?  G  A  A
C  A  A  G  R  S  G  V  Q  P  A  R  G  G  L  L  G  G  G  A  R  A  R  L

CGGGGGCGCCCCYTRAGCAGAAAACAGGRAGAACCAGGCTSGGTCMAGTGGCACCMAGCTCCCTACYTCY 140
GCCCCCGCGGGGRAYTCGTCTTTTGTCCYTCTTGGTCCGASCCAGKTCACCGTGGKTCGAGGGATGRAGR

Below
SUG#301
SUG#313

S  G  A  P  ?  ?  Q  K  T  G  R  T  R  L  G  ?  V  A  P  S  S  L  ?  ?
 R  G  R  P  L  S  R  K  Q  ?  E  P  G  ?  V  ?  W  H  ?  A  P  Y  ?
  G  G  A  P  .  A  E  N  R  ?  N  Q  A  ?  S  S  G  T  ?  L  P  T  S

KGTGCMAGCCGCCTKGCCTGTGGCAGGCCAWTCCCARCGKYCCCGACTGTGACCACTTGCTCAGTGTGCC 210
MCACGKTCGGCGGAMCGGACACCGTCCGGTWAGGGTYGCMRGGGCTGACACTGGTGAACGAGTCACACGG

Below
SUG#301
SUG#313

  V  ?  A  A  ?  P  V  A  G  ?  S  Q  R  ?  R  L  .  P  L  A  Q  C  A
?  C  ?  P  P  ?  L  W  Q  A  ?  P  ?  ?  P  D  C  D  H  L  L  S  V  P
 ?  A  S  R  L  A  C  G  R  P  ?  P  ?  ?  P  T  V  T  T  C  S  V  C
```

Signed: R. Mtr — Date: [redacted]

Read and Understood By

Signed: (signature) — Date: [redacted]

PROJE[redacted]

MKK1-3 consensus 4/12 Map (1 > 2053)Site and Sequence

TCTCACSDGYCYCAKTTTCCCTCTGKGGGGCGATAGGCGSGGCGAGGCTCTCTGGTTTCCTGGCGGGCAT 280

AGAGTGSHCRGRGTMAAAGGGAGACMCCCCGCTATCCGCSCCGCTCCGAGAGACCAAAGGACCGCCCGTA

Below

SUG#301

SUG#313

SUG#304

SUG#304

S H ? ? ? F P S ? G R . A ? R G S L V S W R A
L T ? ? ? F P L ? G D R R G E A L W F P G G H
L S ? ? ? ? S L ? G A I G ? A R L S G F L A G I

TTCACGGCTGTGATTCTGCTGAGGAACTTCCCCGGGTGAGCCCCCGCTTCCTCCGAGCCTGGCACCCCCC 350

AAGTGCCGACACTAAGACGACTCCTTGAAGGGGCCCACTCGGGGGCGAAGGAGGCTCGGACCGTGGGGGG

One_strand

SUG#313

SUG#313

SUG#304

SUG#304

F H G C D S A E E L P R V S P R F L R A W H P P
F T A V I L L R N F P G . A P A S S E P G T P
S R L . F C . G T S P G E P P L P P S L A P P

TCCCGTCTCAGCCAGGATGCCAACGAGGCGCTGGGCCCCGGGCACCCAGTGTATCACCAAATGCGAGCAC 420

AGGGCAGAGTCGGTCCTACGGTTGCTCCGCGACCCGGGGCCCGTGGGTCACATAGTGGTTTACGCTCGTG

One_strand

SUG#313

SUG#313

SUG#304

SUG#304

SUG#301

P V S A R M P T R R W A P G T Q C I T K C E H
L P S Q P G C Q R G A G P R A P S V S P N A S T
S R L S Q D A N E A L G P G H P V Y H Q M R A

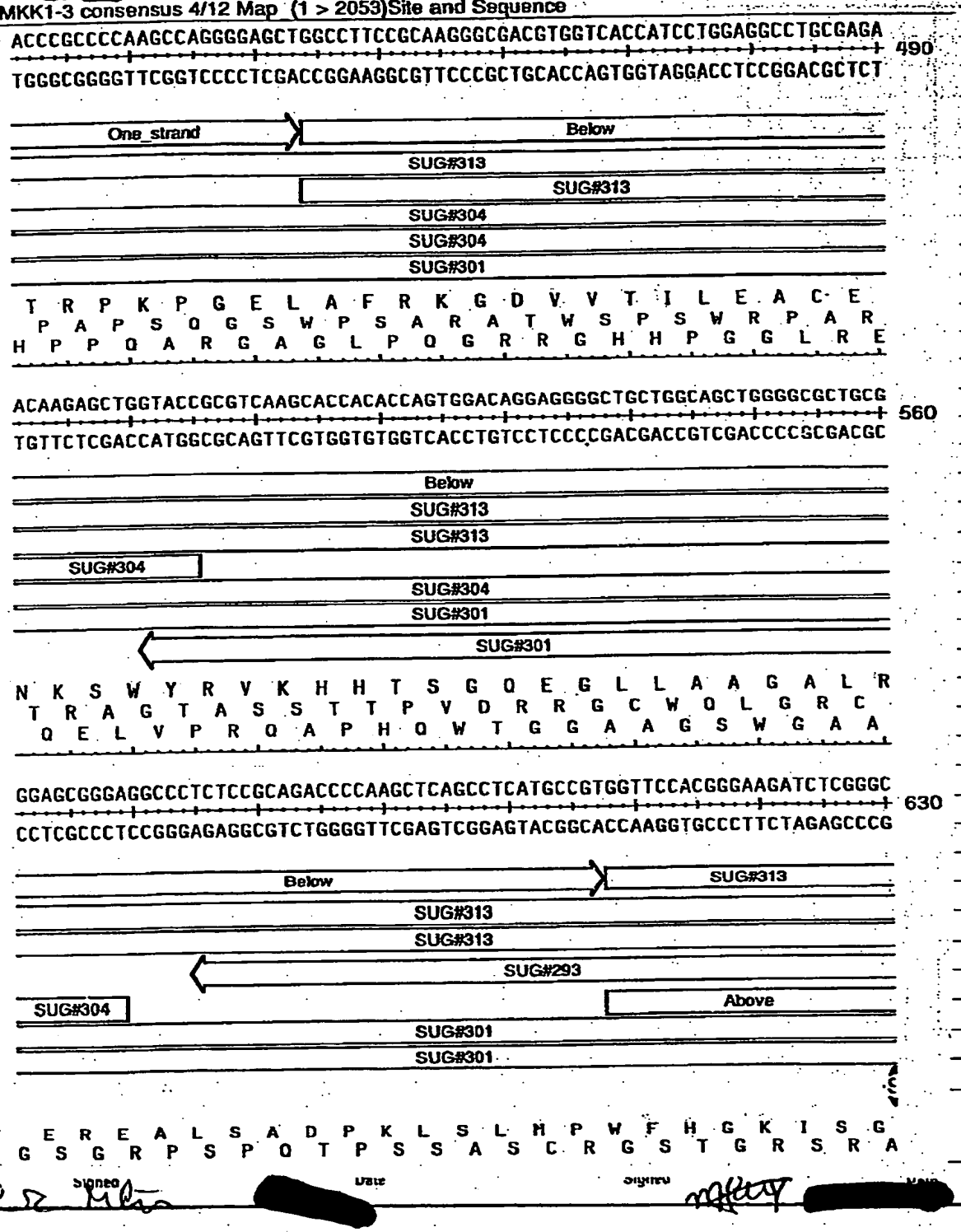
Highlighted residues show identical residues found in human Cyt. (P.2)

RR Mh

*[redacted]

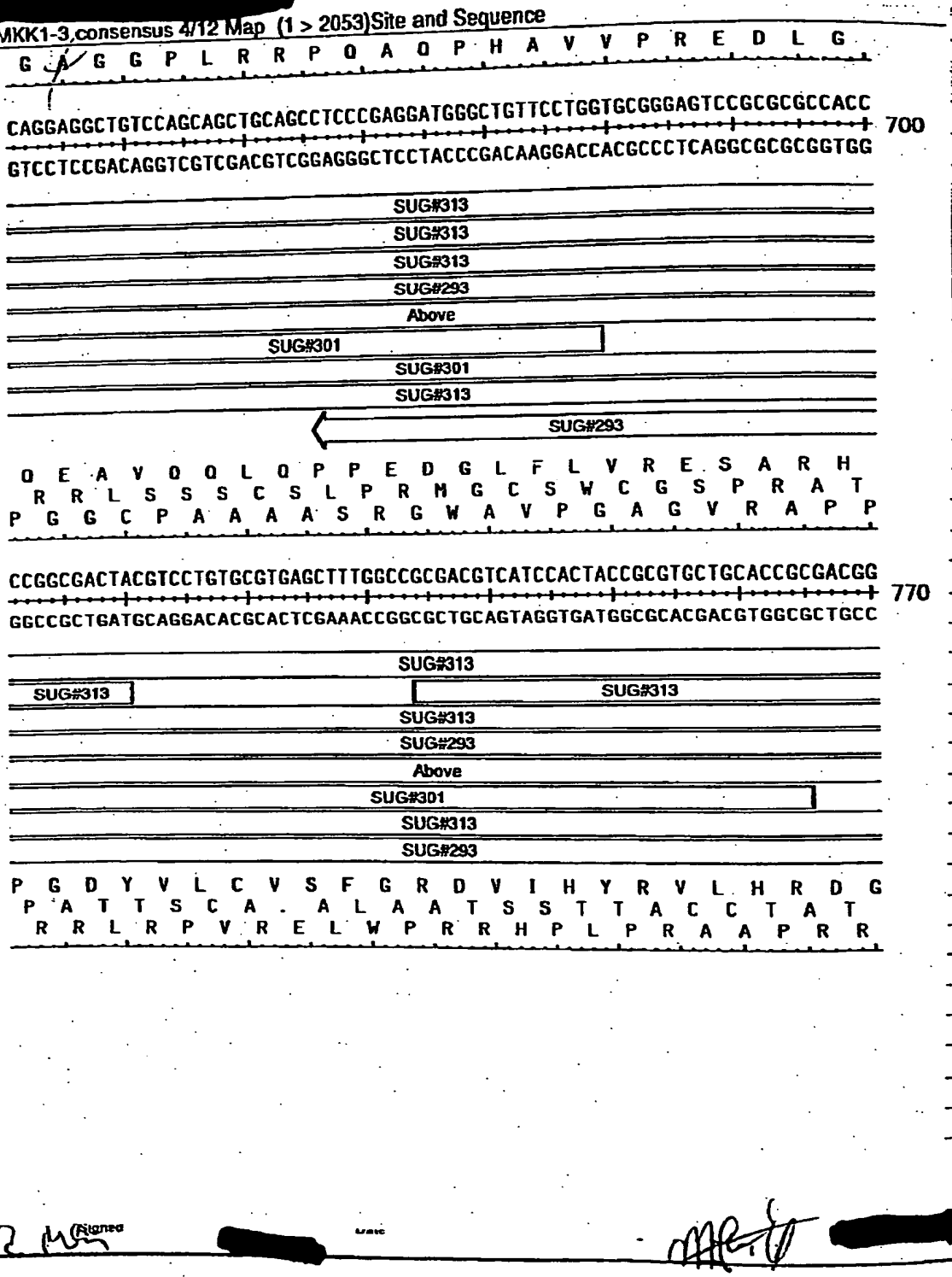
[redacted]

MKK1-3 consensus 4/12 Map (1 > 2053)Site and Sequence



Signed [redacted] Date Signed [redacted]

MKK1-3,consensus 4/12 Map (1 > 2053)Site and Sequence



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MKK1-3 consensus 4/12 Map (1 > 2053)Site and Sequence

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GGTGGAGTGTTAGCTACTCCGGCACAAGAAGACGTTGGAGTACCTGTACCACCTCGTAATGTCGTTCCTG

SUG#313
SUG#313
SUG#313
SUG#293
Above
SUG#313
SUG#313
SUG#293

H L T I D E A V F F C N L M D M V E H Y S K D
A T S Q S M R P C S S A T S W T W W S I T A R T
P P H N R . G R V L L Q P H G H G G A L Q Q G

AAGGGCGCTATCTGCACCAAGCTGGTGAGACCAAAGCGGAAACACGGGACCAAGTCGGCCGAGGAGGAGC 910

TTCCCGCGATAGACGTGGTTCGACCACTCTGGTTTCGCCTTTGTGCCCTGGTTCAGCCGGCTCCTCCTCG

SUG#313
SUG#313
SUG#313
SUG#293
Above
SUG#313
SUG#313
SUG#293

K G A I C T K L V R P K R K H G T K S A E E E
R A L S A P S W . D Q S G N T G P S R P R R S
Q G R Y L H Q A G E T K A E T R D Q V G R G G A

TGGCCAGGGCGGGCTGGTTACTGAACCTGCAGCATTTGACATTGGGAGCACAGATCGGAGAGGGAGAGTT 980

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SUG#313
SUG#313
SUG#313
SUG#282
SUG#293
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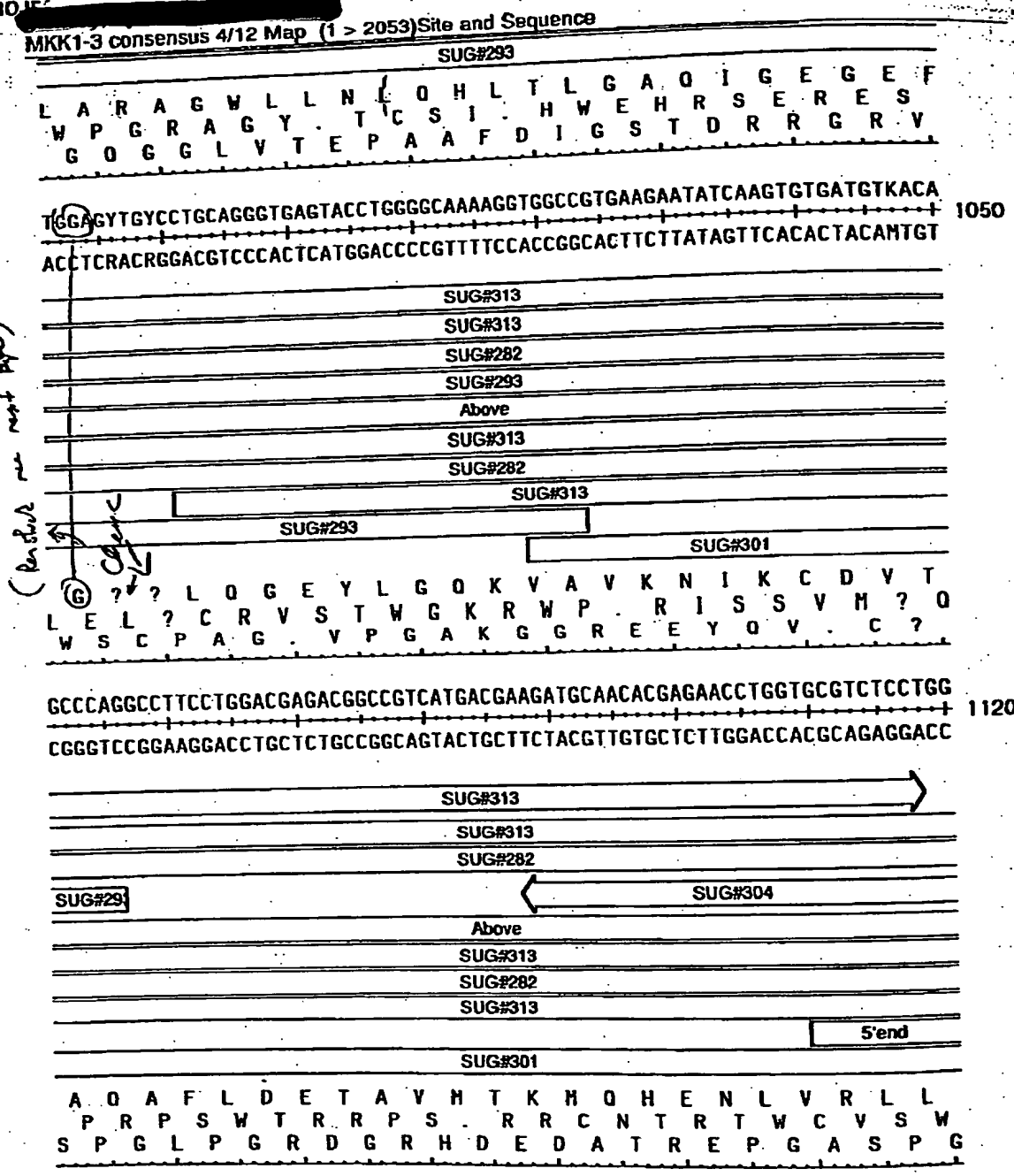
SUG#313
SUG#282
SUG#313

[redacted]

PRO[redacted]

MKK1-3 consensus 4/12 Map (1 > 2053)Site and Sequence

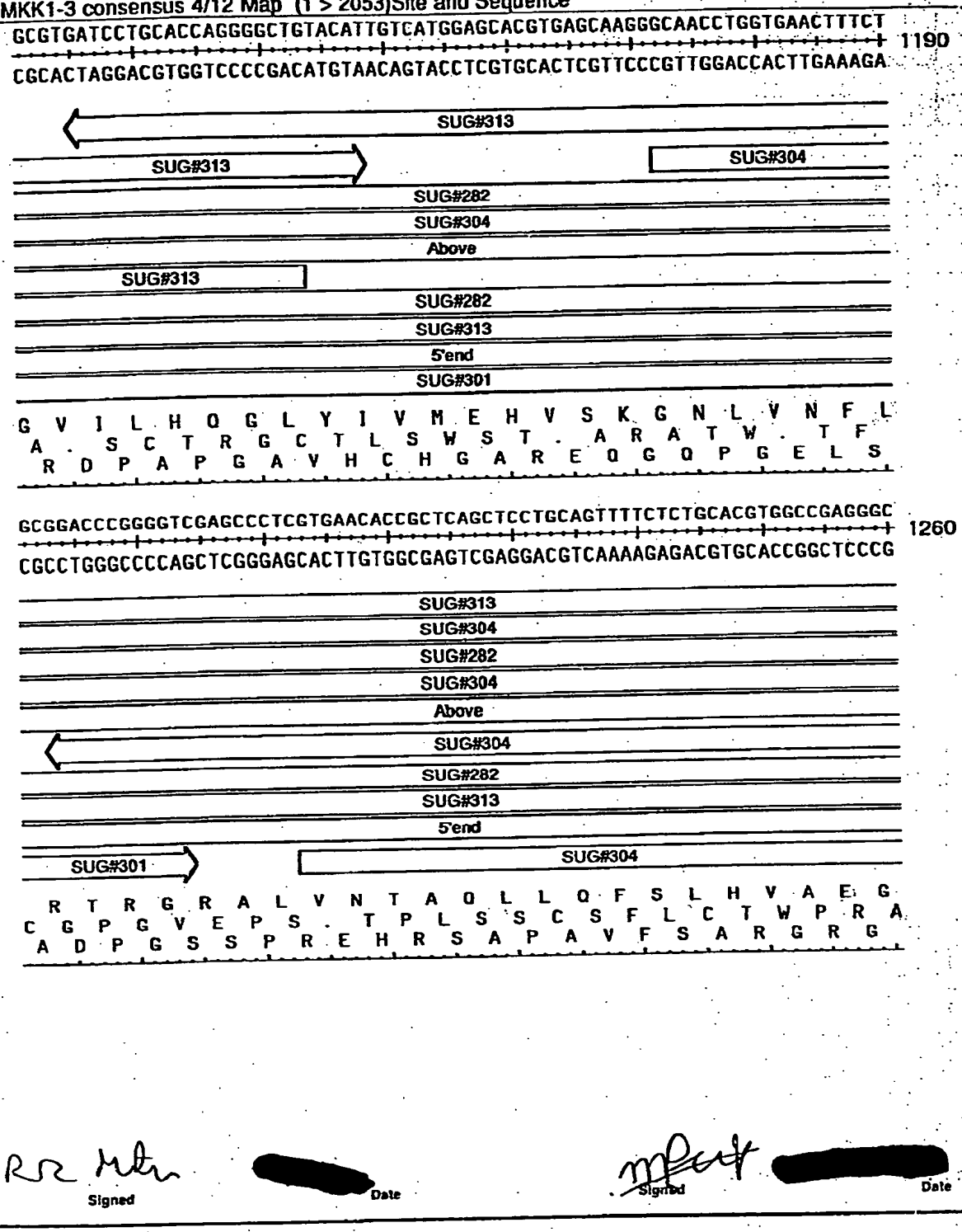


[redacted]

[redacted]

PP [redacted]

MKK1-3 consensus 4/12 Map (1 > 2053)Site and Sequence

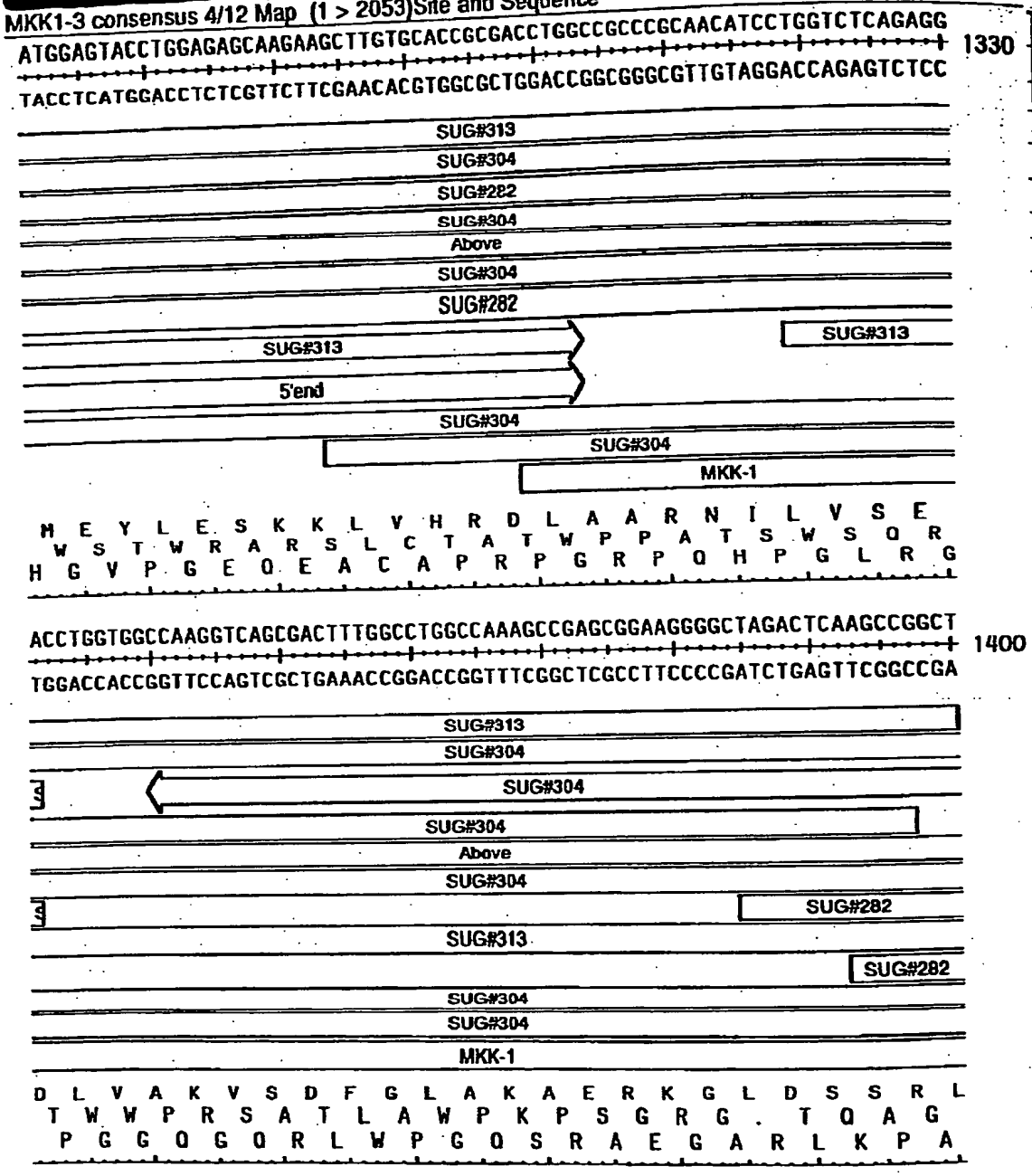


RR Mtn [redacted]
Signed Date

Signed [redacted]
Date

10 [redacted]

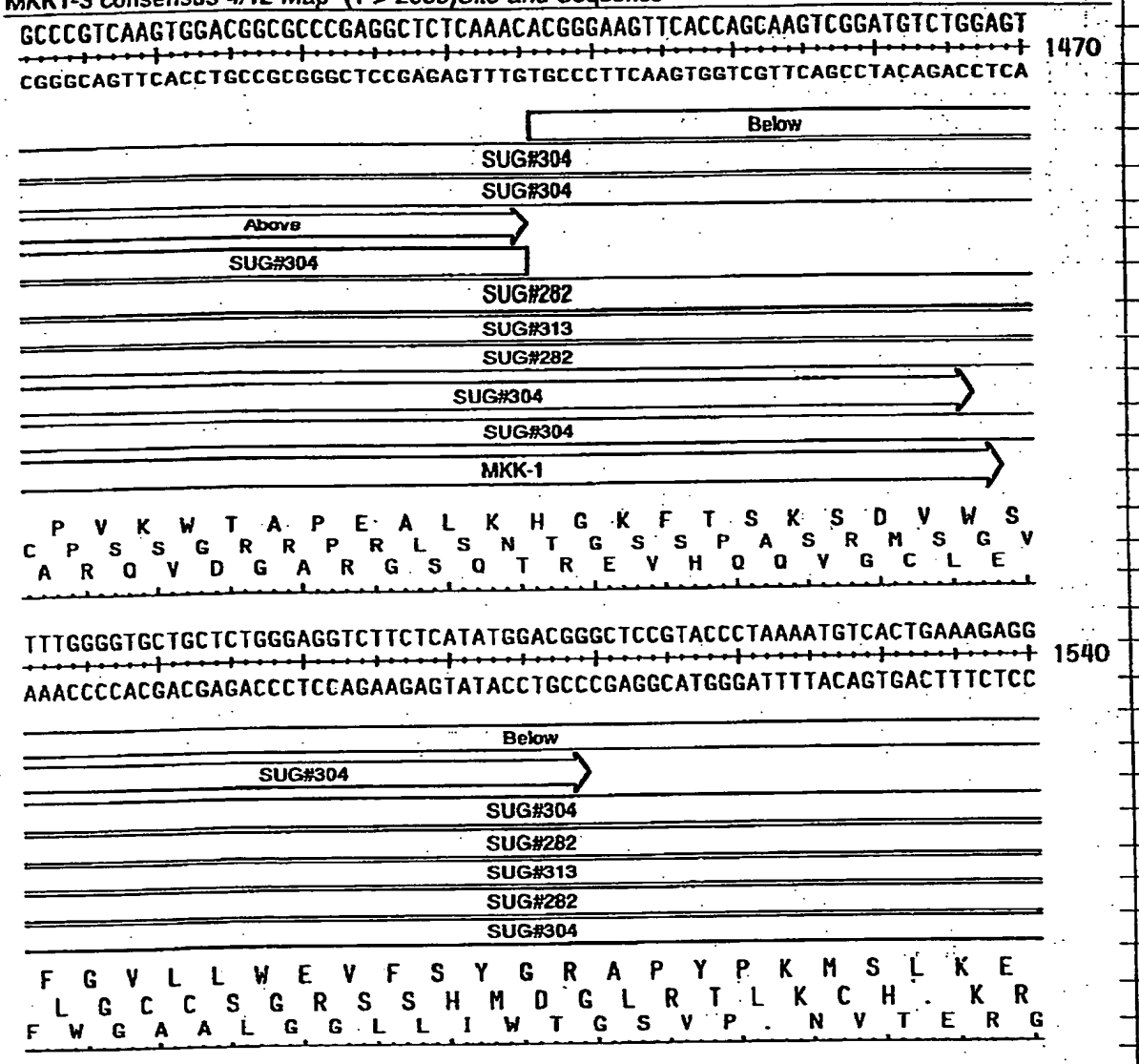
MKK1-3 consensus 4/12 Map (1 > 2053)Site and Sequence



Signed [redacted] Date

Signed [redacted] Date

MKK1-3 consensus 4/12 Map (1 > 2053)Site and Sequence



Signed [redacted] Date

[redacted]

Possible ORF change
Terminates [illegible] 300 a later (see p. 23)

MKK1-3 consensus 4/12 Map (1 > 2053)Site and Sequence

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TGTCGGAGGCCCTGGAGAAGGGGTACCGCATGGAACCCCCCCGAGGGCTGTCCAGGCCCGTGCACGTACT
------------------------------------------------------------------------ 1610
ACAGCCTCCGGGACCTCTTCCCCATGGCGTACCTTGGGGGGGCTCCCGACAGGTCCGGGCACGTGCATGA
```

Below > One_strand
SUG#293
SUG#304
SUG#282
SUG#313 >
SUG#282
SUG#304

```
V  S  E  A  L  E  K  G  Y  R  M  E  P  P  R  G  [circled]  S  R  P  V  H  V  L
 C  R  R  P  W  R  R  G  T  A  W  N  P  P  E  G  C  P  G  P  C  T  Y
  V  G  G  P  G  E  G  V  P  H  G  T  P  P  R  A  V  Q  A  R  A  R  T
```

```
CATGAGCAGCTGCTGGGAGGCAGAGCCCGCCGCCGGCCACCCTTCCGCAAACTGGCCGAGAAGCTGGCCC
------------------------------------------------------------------------ 1680
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```

One_strand > Below
SUG#293
< #267
SUG#293
SUG#282 >
SUG#282
SUG#304

```
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S  C  A  A  A  G  R  Q  S  P  P  P  A  T  L  P  Q  T  G  R  E  A  G  P
 H  E  Q  L  L  G  G  R  A  R  R  R  P  P  F  R  K  L  A  E  K  L  A
```

```
GGGAGCTACGCAGTGCAGGTGCCCCAGCCTCCGTTCTCAGGGCAGGACGCCGACGGCTCCACCTCGCCCC
------------------------------------------------------------------------ 1750
CCCTCGATGCGTCACGTCCACGGGGTCGGAGGCAAGAGTCCCGTCCTGCGGCTGCCGAGGTGGAGCGGGG
```

Below
SUG#293
#267
SUG#293
SUG#282 >
SUG#304

```
G  S  Y  A  V  Q  V  P  Q  P  P  F  S  G  Q  D  A  D  G  S  T  S  P
 G  A  T  Q  C  R  C  P  S  L  R  S  Q  G  R  T  P  T  A  P  P  R  P
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MKK1-3 consensus 4/12 Map (1 > 2053)Site and Sequence

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CTTCGGTCCTCGGGACTGGGGTGGGCCACCCCGGGAACCGGGTCTCCTGGCTCTCTCACCTCTCATGCCG

Below
SUG#293
#267
SUG#293
SUG#304

R S Q E P . P H P V G P L A Q R T E R V E S T A
E A R S P D P T R W G P W P R G P R E W R V R
K P G A L T P P G G A L G P E D R E S G E Y G

GTGGGGGCACTGACCAGGCCCAAGGAGGGTCCAGGCGGGCAAGTCATCCTCCTGGTGCCCACAGCAGGGG 1890
CACCCCCGTGACTGGTCCGGGTTCCTCCCAGGTCCGCCCGTTCAGTAGGAGGACCACGGGTGTCGTCCCC

Below
SUG#293
#267
SUG#293

W G H . P G P R R V Q A G K S S S W C P Q Q G
R G G T D Q A Q G G S R R A S H P P G A H S R G
V G A L T R P K E G P G G Q V I L L V P T A G

CTGGCCCACGTAGGGGGCTCTGGGCGGCCCGTGGACACCCCAGACCTGCGAAGGATGATCGCCCGATAAA 1960
GACCGGGTGCATCCCCCGAGACCCGCCGGGCACCTGTGGGGTCTGGACGCTTCCTACTAGCGGGCTATTT

Below
SUG#293
#267
SUG#293

L A H V G G S G R P V D T P D L R R M I A R .
W P T . G A L G G P W T P Q T C E G . S P D K
A G P R R G L W A A R G H P R P A K D D R P I K

Signed [redacted] Date

[redacted] Date

MKK1-3 consensus 4/12 Map (1 > 2053)Site and Sequence

GACGGATTCTAAGGACTCTAAAAAAAGGGGGGGCCCGGTACCCAATTCGCCCTATAGTGAGTCGTATTAA 2030

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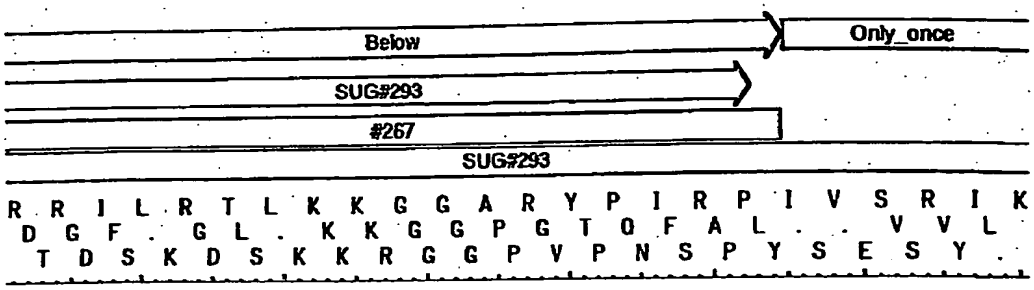
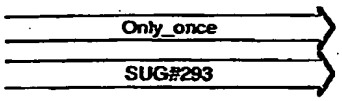


R R I L R T L K K G G A R Y P I R P I V S R I K
D G F . G L . K K G G P G T O F A L . . V V L
T D S K D S K K R G G P V P N S P Y S E S Y .

AATTAACTGGCCGTCGTTTTAAT 2053

TTAATTGACCGGCAGCAAAATTA



I N W P S F .
K L T G R R F N
N . L A V V L M

[redacted]

[redacted]